OCULAR SURFACE DISEASE AMONG PATIENTS WITH OPEN ANGLE GLAUCOMA USING TOPICAL ANTI-GLAUCOMA MEDICATIONS

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ABSTRACT

Objective: To determine the frequency of ocular surface disease among patients with open angle glaucoma using topical anti-glaucoma medications presenting at a tertiary care eye hospital.
Study Design: Cross-sectional analytical study.
Place and Duration of Study: Armed Forces Institute of Ophthalmology, Rawalpindi, from May 2019 to Jan 2020.
Methodology: One hundred and eighty patients aged 18 or more, with open angle glaucoma using any of the topical anti-glaucoma medications including preparations of dorzolamide, brimonidine, timolol, levobunolol, betaxolol, latanoprost, travoprost, bimatoprost or a combination of these for more than six months took part in the study. Ocular surface disease index was used to assess the presence and severity of ocular surface disease.
Results: Out of 180 patients of glaucoma managed with topical anti-glaucoma medications, 83 (46.1%) did not show presence of ocular surface disease when ocular surface disease index was administered. Twenty-nine (16.1%) patients had mild symptoms, 17 (9.4%) had moderate symptoms while 51 (28.3%) patients reported severe symptoms of ocular surface disease. Advancing age and longer duration of treatment with topical anti-glaucoma medications had statistically significant association with the presence of ocular surface disease (p-value <0.05).
Conclusion: Presence of ocular surface disease was a common finding among patients using topical agents for the management of glaucoma. Advancing age and prolonged use of anti-glaucoma medication emerged as risk factors statistically related to the presence of ocular surface disease.

Keywords: Anti-glaucoma drugs, Dry eye syndrome, Glaucoma, Ocular surface disease.

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INTRODUCTION

Ocular diseases affect individuals of all age groups; however, type and presentation may vary.[1] Glaucoma is a commonly diagnosed clinical condition at ophthalmology clinics worldwide.[2] Situation is not different in our part of the world. Incidence and prevalence of glaucoma has been on the rise in Pakistan over the last two decades.[3]

Management of glaucoma depends upon a number of factors including age of the patient, type of glaucoma, underlying pathology, co-morbidities and severity of disease.[4] Topical therapy has been the main stay of treatment for open angle glaucoma and involves medications from various pharmacological groups to lower the intraocular pressure (IOP).[5] Laser trabeculoplasty and various surgical procedures can also be used for adequate control of IOP. All these management options have their own risks and benefits.[6]

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Ocular surface disease (OSD) is an umbrella term encompassing several clinical conditions affecting the surface of the eye.[7] Presence of OSD can adversely affect an individual's visual function and quality of life. Patients with glaucoma have been reported to develop signs and symptoms of OSD. Leung *et al*, performed a study on patients using topical anti-glaucoma drugs and found a high prevalence of OSD in patients with open angle glaucoma and ocular hypertension. The study also suggested that prolonged use of preparations containing preservatives such as benzalkonium chloride may adversely affect vision-related quality of life.[8] A study conducted by Zemba *et al,* reported as many as 63% of glaucoma patients on topical treatment to be suffering from coexistent dry eyes. These patients were found to have poor tear film quality and reduced tear production resulting from long term topical therapy.[9] Barisic *et al,*[10] conducted a study at Croatia involving 160 subjects including 110 patients receiving topical IOP lowering therapy and 50 controls. The study showed that OSD was much more common in patients treated for glaucoma with topical medications

when compared with the control group. Untoward effects of anti-glaucoma agents on ocular surface health may be significant enough to influence comp-liance with glaucoma therapy resulting in treatment failure.

Treatment of glaucoma involves long-term therapy, often with multiple pharmacological agents. Long-term instillation of eye drops poses an increased risk of developing OSD. Adequate estimation of burden of this adverse effect is necessary so that clinicians are able to provide relevant information care to their patients. Moreover, patients may need to be assessed regularly for OSD while using topical anti-glaucoma medications.

While several studies have looked at the presence of OSD with glaucoma in western populations, little work in this regard has been done in Pakistan. Primary aim of conducting this study, therefore, was to determine the frequency of ocular surface disease in patients with open angle glaucoma using topical anti-glaucoma medications presenting at a tertiary care eye hospital in Pakistan. As a secondary objective, the study investigated the correlation between the presence of OSD and advancing age, gender, duration of treatment as well as number of topical IOP lowering medications.

METHODOLOGY

This cross-sectional analytical study was conducted at Armed Forces Institute of Ophthalmology, Rawalpindi from May 2019 to January 2020. Approval of hospital ethical review committee was taken vide certificate reference number 220/ERC/AFIO. Sample size was calculated by using the WHO sample size calculator with a population prevalence proportion of 72.4%.[7] Non-probability consecutive sampling was used for patients of open angle glaucoma who were using topical anti-glaucoma medications reporting in the outpatient department of Armed Forces Institute of Ophthalmology, Rawalpindi after obtaining informed consent. Open angle glaucoma was previously diagnosed by a consultant ophthalmologist on the basis of clinical criteria supported by relevant investigations.[11,12] Management decisions were also made and reviewed by a consultant ophthalmologist on each visit.

Inclusion Criteria: Patients of age 18 years or more with primary, secondary or juvenile open angle glaucoma using any of the topical anti-glaucoma medications including preparations of dorzolamide, brimonidine, timolol, levobunolol, betaxolol, latanoprost, travoprost, bimatoprost or a combination of these for six months or more were included in the study.

Exclusion Criteria: Patients with active ocular infection, history of ocular inflammatory disease, prior corneal or refractive surgery, dry eye syndrome, contact lens use within the last 30 days and current use of topical corticosteroids, topical non-steroidal anti-inflammatory drugs or cyclosporine ophthalmic emulsion were also excluded.

The Ocular Surface Disease Index (OSDI) is a simple and easy to administer tool which can be used to assess the presence and severity of OSD. It is a validated tool with 12 points, divided into three subscales: ocular symptoms, vision-related function and environmental triggers. It has a total scoring range from 0-100. OSDI scores of 0-12 were considered normal; scores ranging from 13-22 were classified as mild, 23-32 as moderate and 33-100 as severe disease.[13]

After getting approval from the hospital ethical review board committee, OSDI questionnaire translated in Urdu was administered to patients under the supervision of a health care professional. Ambiguity regarding any point in the questionnaire was clarified. Participants were asked to answer the questions according to their condition over the last week. Detailed history taking and review of medical record possessed by the patients was carried out. Relevant socio-demographic factors were recorded in a proforma attached to OSDI questionnaire.

Statistics Package for Social Sciences version 24 was used to perform all statistical analyses. Characteristics of study participants and distribution of OSDI score were reported using descriptive statistics. The study looked at various variables including age and gender of the participants, duration of treatment with topical agents and use of more than one drug. Between-group variances in categorical correlates were determined using Pearson's chi-square test. The *p*-value ≤0.05 was considered significant for all tests.

RESULTS

A total of 180 patients participated in the study analysis. Out of these 180 patients of glaucoma were managed with topical anti-glaucoma medications, 83 (46.1%) did not show presence of ocular surface disease when OSDI was administered. Mean age of the study participants was 54.94 ± 7.19 years and mean duration of glaucoma among the patients in this study was 3.12 ± 2.48 years shown in Table-I. 29 (16.1%) patients had mild, 17 (9.4%) had moderate while 51 (28.3%) patients had severe symptoms of OSD (Figure).

Table-I: Characteristics of study participants.

Parameters	Values
Age	
Mean ± SD	54.94 ± 7.19 years
Range (min-max)	20-70 years
Gender	
Male	130 (72.2%)
Female	50 (27.8%)
Mean duration of Glaucoma	3.12 ± 2.48 years 6 months - 5 years
Symptom of Ocular Surface Disease	
Dryness	57 (31.6%)
Soreness	41 (22.7%)
Grittiness	33 (18.3%)
Blurring/poor vision	29 (16.1%)
Tearing	16 (8.8%)
Light sensitivity	15 (8.3%)
Difficulty driving at night	11 (6.1%)
Others (difficulty reading or watching TV etc)	59 (32.7%)

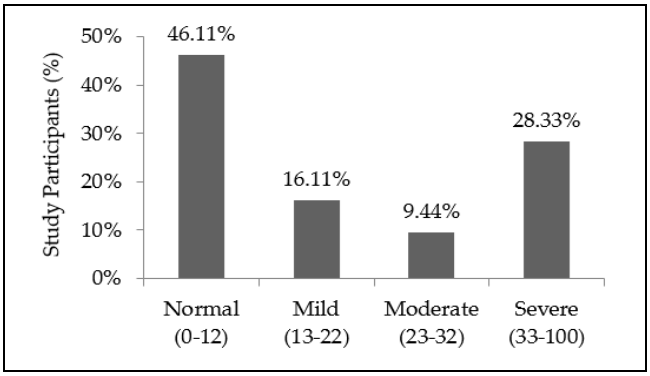

Figure: Histogram showing severity distribution of ocular surface disease index scores.

Table-II shows that advancing age (p=0.041) and longer duration of treatment with topical anti-glaucoma (p=0.006) medications had statistically significant association with the presence of OSD (p<0.05) when Pearson's chi-square test was applied. Gender (p=0.312) and use of more than one topical anti-glaucoma agent did not have any statistically significant relationship with the presence of OSD in the study participants (p=0.384).

DISCUSSION

Iatrogenic harm has always been an area of concern for clinicians and researchers. The risks and benefits of all treatment options need to be weighed before initiation of treatment. Ophthalmology is no exception to this rule. Glaucoma is a group of disorders having characteristic cupping of the optic disc with corresponding visual field defects. Topical IOP lowering medications remain the mainstay of treatment in most of the cases.[14] Preservatives used in these medications as well as some of the active ingredients are known to cause chronic inflammation of the ocular surface. Patients with glaucoma typically receive treatment for many years to decades. OSD caused or aggravated by topical medication may result in poor adherence to or even discontinuation of glaucoma treatment. Moreover, untreated ocular surface disease may significantly affect patients' quality of life. Therefore, it is essential that clinicians are aware of this adverse drug effect in order to be able to provide adequate information and care to their patients.

Dubrulle *et al*,[15] conducted a study in France with the objective to look for the effect of treating OSD in patients with medically uncontrolled primary open angle glaucoma (POAG) associated with OSD. The study concluded that the prevalence of OSD in POAG patients is high, particularly in patients with uncontrolled glaucoma using multiple topical medications. Careful management of the ocular surface associated with a reduction of the toxicity of eye drops may result in improvement of ocular surface health and better intraocular pressure control.

Asiedu *et al*,[16] published a comprehensive review on this subject and summarized that preservatives and

Table-II: Comparison between ocular surface disease index score of study participants.

Socio-Demographic Factors	No Ocular Surface Disease	Mild Ocular Surface Disease	Moderate Ocular Surface Disease	Severe Ocular Surface Disease	p-value
Age					
18-50	41 (49.4%)	13 (44.8%)	02 (11.8%)	21 (41.2%)	0.041
>50	42 (50.6%)	16 (55.2%)	15 (88.2%)	30 (58.8%)	
Gender					
Male	58 (69.9%)	18 (62.0%)	14 (82.3%)	40 (78.4%)	0.312
Female	25 (30.1%)	11 (37.9%)	03 (17.6%)	11 (21.6%)	
Duration of Treatment					
<2 years	52 (62.7%)	18 (62.0%)	06 (35.3%)	18 (35.3%)	0.006
>2 years	31 (37.3%)	11 (37.9%)	11 (64.7%)	33 (64.7%)	
Number of Drugs					
One	24 (28.9%)	07 (24.1%)	07 (41.2%)	20 (39.2%)	0.384
More than one	59 (71.1%)	22 (75.9%)	10 (58.8%)	31 (60.8%)	

active agents in most topical glaucoma medications are implicated in affecting the integrity of the ocular surface. As the prime aim of management remains the preservation of vision, ocular surface assessment is often overlooked. The discomfort experienced by glaucoma patients due to poor ocular surface health cannot only terribly affect their quality of life, but also has an impact on overall glaucoma prognosis. Clinicians involved in glaucoma care should adopt a proactive approach towards the assessment of ocular surface and management of OSD.

Advancing age was related to presence of OSD in various studies done in the past. Study by Saini *et al*. published in 2018 is important in this regard.[17] This factor needs further exploration and that too by case/ control or cohort studies since senile changes may predispose an individual to OSD.

Increased duration of glaucoma and prolonged use of anti-glaucoma medications was found to be a consistent correlate with the presence and severity of OSD. Lee *et al*.[18] published in 2019 that patients in South Korea with glaucoma using topical anti-glaucoma medications have increased chances of having abnormalities of the ocular surface. Increased duration of disease has a positive correlation with the presence of OSD. Findings of our study and those of Lee *et al*. indicate that either disease process of glaucoma or the use of anti-glaucoma drugs has a clear role in precipitation of OSD.

LIMITATION OF STUDY

Cross-sectional study design was the main limitation of our study. Cause-effect relationship could not be established with this design. In addition, patients did not undergo clinical examination for OSD or OSDI scoring before commencement of anti-glaucoma therapy. Furthermore, relationship between type of medication and symptoms of OSD could not be assessed as patients had been switching between various medications over different periods of time. Future studies addressing these limitations may prove beneficial.

CONCLUSION

Presence of OSD is a common finding among patients using topical IOP lowering agents for the management of glaucoma. Advancing age and longer duration of treatment emerged as risk factors statistically related to the presence of OSD. Clinicians need to adopt a proactive approach for early detection and appropriate management of coexisting OSD in glaucoma patients.

Conflict of Interest: None.

Authors' Contribution

HJ: Conception, data collection, analysis & manuscript drafting, OZ: Research supervision and final approval, SA: Manuscript drafting, SA: Statistical analysis & interpretation, IUK: Conception & reserch analysis.

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